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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/016,825	11/09/2001	Harvey A. Schwertner	AFD 489	9046

26902 7590 10/06/2003

DEPARTMENT OF THE AIR FORCE
AFMC LO/JAZ
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EXAMINER	
SHARAREH, SHAHNAM J	

ART UNIT	PAPER NUMBER
1617	4

DATE MAILED: 10/06/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/016,825	Applicant(s) SCHWERTNER ET AL.	
	Examiner Shahnam Sharareh	Art Unit 1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 November 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 2* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 2* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Claims 1-2 are pending.

Specification

2. The disclosure is objected to because of the following informalities:

Paragraph 2 incorporates related applications. Clarification of the serial Number is requested.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 2 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The limitations "now" and "severe" in claim 2 are relative terms, which render the claim indefinite. Neither of the terms are defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 1-2 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schwertner US Patent 5,380,667 and Kannel et al (Ann. Intern. Med. 90:85-97, 1979).

The pending claims are directed to methods of characterizing the risk of Coronary Artery Disease ("CAD" or "CHD") [1] for an individual comprising obtaining levels of the individual's LDL-cholesterol (LDL-C), HDL-cholesterol (HDL-C), and serum total bilirubin and then comparing a ratio of LDL-C/(HDL-C + total bilirubin) to a predetermine level for that ratio. Examiner points out that the step (c) of claim 1 is a non-limiting step, because by performing steps (a) and (b) the risk of the CAD is already established.

In short, step (c) is a non-functional step, because it cannot alter the process steps of the pending claims to achieve the utility of the invention. Therefore, for applying prior art the

nonfunctional and descriptive limitation of step (c) is not given patentable weight. (see MPEP 2106, VI for description of a non-functional process step).

Schwertner teaches that CAD risk is directly related to total cholesterol levels and further inversely associated with bilirubin and HDL-C levels. Schwertner methods of predicting CAD comprise the first step of measuring levels of serum bilirubin, HDL-C and total cholesterol. (col 4, lines 60-col 8, line 40). Schwertner then suggest the use of serum bilirubin as the predictor for CAD (col 10, lines 60-67). Schwertner finally introduces a new formula for predicting CAD wherein a ratio of total cholesterol to bilirubin is calculated for each individual and then the calculated ratio is compared to a predetermined threshold level. (col 12, lines 39-51). Schwertner reports its parameters in such way that the ratio is a whole number. (see col 10, lines 44-54).

Schewertner also acknowledges the conventional method of predicting the risk of CAD wherein individual's total cholesterol and HDL-C is first measured and then expressed in a ratio of total cholesterol / HDL-C (see col 2, lines 10-15). Accordingly, Schwertner teachings provide that the risk of CAD has an inverse relationship with the bilirubin and HDL-C.

Schwertner's formula fails to explicitly use LDL-C in the numerator and the sum of the HDL-C and bilirubin levels in its denominator.

4. Kannel provides that LDL-C is superior to the total cholesterol as a measure of atherogenic cholesterol (see page 89, 6th para). Kannel describes LDL-C as a powerful predictor of the risk of CHD in human subjects and that elevated levels of LDL are associated with increased risk of CHD (see page 87, 3rd para. and para.9). Kannel describes the outcome of Framingham Study (1971) ("the Study") and concludes that the Study shows a clear correlation

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[1] The Term CAD, Coronary Heart Disease (CHD) and Arteriosclerotic Heart Disease are used interchangeably as they are art recognized alternative terminologies. See the attached definition provided by Kernan Hospital, University of Maryland Health Systems. ~~com/ency/article/007115.htm~~

between risk for CHD and serum cholesterol levels (abstract). Kannel does not discuss the use of bilirubin as a predictor of CHD.

5. The combined teachings of Schwertner and Kannel provide that the risk for developing CAD is a function of HDL-C, LDL-C, total cholesterol, and bilirubin. Therefore, these parameters are viewed to be well-recognized "result-effective variables" for assessing the risk of developing CAD. (see MPEP 2144.05 II.B for definition of "Result Effective Variables")

6. While the value of LDL-C in the numerator, and the sum of the values for HDL-C and bilirubin in the denominator are not directly used by Schewertner formula, it would have been obvious to one of ordinary skill in the art at the time of invention to increase the diagnostic sensitivity of Schewertner's formula by optimizing these values in the numerator and denominator of Schewertner's formula through a simple statistical experimentation wherein LDL-C is used in the numerator and the sum of HDL-C and bilirubin is used in the denominator.

7. One of ordinary skill in the art would have been motivated to substitute the total cholesterol in Schwertner's formula with LDL-C value, because as taught by Kannel, LDL is a superior to total cholesterol as an indicator of CAD.

8. The ordinary skill in the art would have further been motivated to account for both values of HDL-C and bilirubin in the denominator, because as described by Schwertner bilirubin and HDL-C are recognized indicators of CAD risk that have inverse relationship with such risk. Therefore, to best characterize the correlation between these values and the risk of developing CAD, summing the HDL-C and bilirubin values in the denominator as a means to optimize Schwertner's formula would have been a matter of routine statistical experimentation.

Conclusion

No claims are allowed. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shahnam Sharareh whose telephone number is 703-306-5400. The examiner can normally be reached on 8:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, PhD can be reached on 703-308-1877. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1123.

Shahnam Sharareh, PharmD
Patent Examiner
Art Unit, 1617

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